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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/446,317	04/17/00	WAGNER	E 0652.2010000

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EXAMINER	
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ART UNIT	PAPER NUMBER
1632	13

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/446,317	WAGNER ET AL.	
	Examiner	Art Unit	
	Richard Schnizer	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2000* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☐ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *8,11* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other: .

DETAILED ACTION

Continued Prosecution Application

The request filed on 12/29/00 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09/446,317 is acceptable and a CPA has been established. An action on the CPA follows.

Two Information Disclosure Statements and preliminary amendment were received and entered as Paper Nos. 8, 11 and 12, respectively, on 12/29/00 and 1/17/01. Claims 35-68 remain pending and are under consideration in this Office Action.

Rejections Withdrawn

The rejection of claims 58-63 under 35 U.S.C. 103 is withdrawn in view of Applicant's arguments regarding the order of addition of the hydrophilic polymer to PEI.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 53-57 and 65-68 stand rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled

in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention for the reasons of record in Paper No. 5.

Claims 53-57 are drawn to a composition comprising a therapeutically active nucleic acid. Claims 65-68 are drawn to a pharmaceutical composition comprising a nucleic acid. For the purpose of examination under 35 U.S.C. 112, first paragraph, "pharmaceutical compositions", and compositions comprising therapeutically active substances, must be enabled for therapeutic use. Thus, the specification must support a therapeutic embodiment for claims 53-57 and 65-68, particularly in light of the specification at page 1, lines 21-24; and page 4, lines 23-26. Because these claims are drawn to therapeutic nucleic acids and pharmaceutical compositions wherein the active ingredient is a nucleic acid, the specification must enable nucleic acid-mediated therapy.

At the time the invention was made, successful implementation of gene therapy protocols was not routinely obtainable by those skilled in the art. This is reflected by two recently published reviews. Verma et al (1997) teach that "there is still no single outcome that we can point to as a success story (p. 239, col 1). The authors state further, "Thus far, the problem has been the inability to deliver genes efficiently and to obtain sustained expression" (p.239, col. 3). Anderson (1998) states that "there is still no conclusive evidence that a gene-therapy protocol has been successful in the treatment of human disease" (p. 25, col. 1) and concludes, "Several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered" (p.30).

The invention addresses the issue of gene delivery. However no evidence is presented which would convey to a skilled artisan that the art-recognized problems associated with either gene delivery or gene expression have been solved, and the issue of expression after delivery does not appear to have been addressed.

The physiological art in general is acknowledged to be unpredictable (MPEP 2164.03). In the case of gene therapy in general, the art-accepted problems associated with gene delivery and expression result in a very low predictability of success.

Because gene therapy cannot be practiced with routine success by those of skill in the art, and due to the level of unpredictability of the art, and the lack of examples and guidance in the specification, a skilled artisan would have to perform undue experimentation in order to perform gene therapy with the claimed compositions.

Response to Arguments

Applicant's arguments filed 1/17/00 have been fully considered but they are not persuasive.

Applicant indicates that claims 53-57 and dependent claims 65-68 are not drawn to methods of gene therapy, but rather to complexes or pharmaceutical compositions comprising a therapeutically active nucleic acid. Applicant asserts that the fact that the composition may express a therapeutically active protein does not convert the complex into a gene therapy method.

In response, the examiner asserts that the claims clearly require a therapeutic nucleic acid. A simple definition of a therapeutic nucleic acid is one which can be administered to successfully

treat a disease. If a nucleic acid cannot be used to provide therapy, then it is not a therapeutic nucleic acid. As noted above, and in Paper No. 6, the successful use of nucleic acids in methods of therapy is not routine in the art due to problems with delivery, targeting, and expression. In response, Applicant has provided four examples of gene therapy from the prior art, none of which uses a delivery composition remotely resembling the instant invention. The Examiner acknowledges that scattered successes in gene therapy have been obtained. However, the claims broadly encompass gene therapy of any disease, with any gene, in any animal. The fact remains that the state of the art does not support broad claims to therapeutic or pharmaceutical compositions in which the active agent is simply a "therapeutic nucleic acid." As indicated by Verma and Anderson, the overwhelming majority of gene therapy experiments fail due to poor delivery and expression of genes. It therefore falls to the specification to supply that which is missing from the prior art, *e.g.* guidance with respect to the delivery and expression of genes in a manner that allows a therapeutic result. Applicant points to examples 10 and 12 which demonstrate that the addition of PEG to the complexes stabilizes them, and that the addition of a targeting ligand improves their delivery to a target tissue, but fails to point to a single working example of therapy in the specification. Applicant correctly points out that the invention would be enabled if the specification disclosed at least one method for making and using the invention that bears a reasonable correlation to the entire scope of the claims. In this case, the scope of the claims encompasses gene therapy, and Applicant has not disclosed a single method for the therapy of any condition or disease, and has not made a convincing case that the instant invention can be

used to solve the art-recognized problems facing gene therapy. The mere fact that PEI/DNA complexes can be used to deliver genes *in vivo* does not set these complexes apart from liposomes, retroviral vectors, naked DNA or any other composition which has failed to function as a generally acceptable vector for therapeutic gene delivery.

Because neither the prior art nor the specification provides sufficient guidance for the reasons set forth above and in Paper No. 6, one of skill in the art could not use the claimed compositions as intended without undue experimentation, and the rejection is maintained.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 58-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "dilute" in claims 58-63 is a relative term which renders the claim indefinite. The term "dilute" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and the term does not specify an art-recognized concentration. Specifically, the term "dilute" renders indefinite the concentration of DNA and PEI solutions which must be mixed in the method. Thus the artisan would not reasonably realize the metes and bounds of the invention.

Claims 59 and 60 are indefinite because it is unclear whether the recited DNA concentrations are starting concentrations or final concentrations. Does the recited DNA concentration refer to the solution of DNA which is used to make the composition, or to the concentration of DNA in the final composition?

Claims 61 and 62 are indefinite because it is unclear what salt concentration is intended by "physiological value". Physiological salt concentrations vary with the organism in consideration. For example, halophiles tend to have higher physiological salt concentrations than mammals. These claims are also indefinite because it is unclear what is intended by the phrase, "the complexing is carried at a salt concentration", etc. Insertion of the word "out" after the word "carried" is suggested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 35-43 and 49 stand rejected under 35 U.S.C. 102(e) as being anticipated by either one of Yin et al (US Patent 5,919,442, effective filing date 8/11/95) or Tomalia et al (US Patent 5,714,166, filed 3/7/95) for the reasons of record in Paper No. 6.

Yin teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 5, lines 46-48; column 12, lines 27-37; column 20, lines 20-57, especially lines 47-50; paragraph bridging columns 27 and 28; column 48, claim 8; and column 49, claim 12. A variety of phosphate to nitrogen ratios are encompassed. See column 29, lines 12-19. The molecular weight of PEI may be from 10,000 to 100,000,000. See column 7, lines 32-41. The hydrophilic polymer may be polyethylene glycol, polyvinylpyrollidone, polyacrylamide, or combinations thereof. See column 5 lines 44-50; and claim 12, column 48. The complexes may comprise a targeting ligand attached to PEI. See column 18, lines 41-43; column 54, claim 41; and column 57, claim 63.

Thus Yin anticipates the claims.

Tomalia teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 4, lines 25-32; paragraph bridging columns 13 and 14; column 22, lines 36-40; and column 48, lines 16-25. A variety of phosphate to nitrogen ratios are encompassed. The molecular weight of PEI may be about 2000 D. See column 70, lines 30-34. The hydrophilic polymer may be polyethylene glycol. The complexes may comprise a targeting ligand attached to PEI. See column 22, lines 15-26, paragraph bridging columns 22 and 23, especially column 23, lines 5-10.

Thus Tomalia anticipates the claims.

Claims 35, 41-45, 49, and 52 are rejected under 35 U.S.C. 102(e) as being anticipated by Bogdanov et al (US Patent 5,871,710, effective filing date of 6/17/94) for the reasons of record in Paper No. 6..

Bogdanov teaches a drug delivery composition comprising PEI to which PEG has been covalently attached as a protectant. Polynucleotides may be present as a block copolymer with PEG. See column 5, lines 10-16, and 59-66. The composition may also comprise a targeting group bound to either PEI or PEG. See column 6, lines 36-40. PEG may be present in a molecular weight from 500-10,000 D. See column 15, lines 47-50.

Response to Arguments

Applicant's arguments filed 1/17/01 have been fully considered but they are not persuasive.

Applicant argues that Yin and Tomalia do not teach normal branched chain or linear polymer PEI or that they teach away from such forms of PEI. These arguments are irrelevant because the claims do not recite normal branched chain or linear PEI, and the specification provides no limiting definition with regard to the nature of the PEI which may be used in the instant invention. The instant claims are sufficiently broad to encompass the compositions of both Yin and Tomalia.

Applicant argues that the Examiner has provided no evidence as to why one skilled in the art would be led to the claimed complex as opposed to the many other complexes encompassed by Yin. Applicant's attention is directed to claim 12 of Yin which specifically recites a PEI

polymer which is modified by grafting of a hydrophilic polymer such as PEG, polyacrylamide, or polyvinylpyrrolidone. Additionally, Claim 4 recites that these compositions can be used to carry genetic material. Thus Yin specifically claims materials which are encompassed by the instant claims.

Applicant argues that neither Yin nor Tomalia teach covalent attachment of PEG to PEI. Yin teaches "grafting" of PEG to PEI. Within the context of the specification, "grafting" clearly means covalent attachment. See, for example, Fig. 14, step 3. Tomalia teaches that PEG is "attached" to PEI. The specification clearly indicates that "attachment" encompasses covalent linkage. See column 17, lines 45-48.

Applicant argues that Yin teaches away from the claimed invention because complexes in which PEOX was grafted to PEI did not perform as well as others. In response, the examiner asserts that Yin does not show that these complexes where inoperable. On the contrary Yin shows that such complexes functioned to transfect cells. See Fig. 29 (HCB G0 50% PEOX 50G0 1:200). For this reason Yin does not teach away from the claimed invention.

Applicant argues that Tomalia teaches a core comprising a chemical structure in addition to PEI. This is irrelevant because the instant claims do not preclude such a structure.

Applicant argues that Bogdanov does not teach complexing graft copolymer adducts with DNA. In response, the examiner asserts that Bogdanov teaches complexes of nucleic acid, PEI and a hydrophilic polymer, as required by the claims. Specifically, Bogdanov teaches a block copolymer of PEG and nucleic acids which is covalently attached to PEI. This is considered to be

a complex. Neither the claim nor the specification teaches that a complex cannot be covalent in nature.

For these reasons the rejections are considered to be proper and are maintained.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 44-51 and 64 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Yin et al (US Patent 5,919,442, effective filing date 8/11/95) or Tomalia et al (US Patent 5,714,166, filed 3/7/95), either one in view of Szoka (US Patent 5,661,025, filed 6/7/95) for the reasons of record in Paper No. 6.

Yin teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 5, lines 46-48; column 12, lines 27-37; column 20, lines 20-57, especially lines 47-50; paragraph bridging columns 27 and 28; column 48, claim 8; and column 49, claim 12. A variety of phosphate to nitrogen ratios are encompassed. See column 29, lines 12-19. The molecular weight of PEI may be from 10,000 to 100,000,000. See column 7, lines 32-41. The hydrophilic polymer may be polyethylene glycol, polyvinylpyrollidone, polyacrylamide, or combinations thereof. See column 5 lines 44-50; and

claim 12, column 48. The complexes may comprise a targeting ligand attached to PEI. The targeting ligand may be a protein, and more specifically a hormone. See column 18, lines 41-43; column 54, claim 41; and column 57, claim 63. DNA may be added to PEI in a solution of water comprising about 50 μg DNA/ml. See column 29, lines 39-41. The solution may be diluted for later use. See column 29, lines 35-39.

Yin is silent with respect to the molecular weight of the hydrophilic polymer, the ratio of hydrophilic polymer to PEI primary amine groups, and the order in which the DNA and the hydrophilic polymer are added to PEI. Yin does not teach transferrin or EGF as targeting ligands.

Tomalia teaches complexes comprising a nucleic acid and PEI, wherein PEI is covalently modified with a hydrophilic polymer. See Abstract; column 4, lines 25-32; paragraph bridging columns 13 and 14; column 22, lines 36-40; and column 48, lines 16-25. A variety of phosphate to nitrogen ratios are encompassed. The molecular weight of PEI may be about 2000 D. See column 70, lines 30-34. The hydrophilic polymer may be polyethylene glycol. The complexes may comprise a targeting ligand attached to PEI. The targeting ligand may be a protein. See column 22, lines 15-26, paragraph bridging columns 22 and 23, especially column 23, lines 5-10. DNA may be added to PEI in a solution of water comprising about 50 μg DNA/ml, and then diluted to a concentration of 1-10 μg DNA/ml. See column 49, lines 37-42.

Tomalia is silent with respect to the molecular weight of the hydrophilic polymer, the ratio of hydrophilic polymer to PEI primary amine groups, and the order in which the DNA and the

hydrophilic polymer are added to PEI. Tomalia does not teach transferrin or EGF as targeting ligands.

Szoka teaches a self-assembling polynucleotide delivery system comprising dendrimer polycations. The dendrimers are composed of cationic polyamines similar to polyethylenimine. See column 10, lines 36-46. The complexes may comprise a DNA masking agent, such as PEG, covalently linked to the dendrimer. The PEG may have a molecular weight from 700-20,000 D, and may be present in a ratio of moles of polymer:PEI primary amino groups from 1:3 to 1:33. See column 12, lines 18-43. Szoka also encourages the use of EGF as a targeting ligand, and discloses that transferrin is well known in the art as a targeting ligand. See column 2, lines 43-45; column 3, lines 40-44; and column 14, lines 8-11.

It would have been obvious to one of ordinary skill in the art at the time of the invention to use PEG in the inventions of either Yin or Tomalia in the molecular weights and ratios taught by Szoka. Yin and Tomalia are silent on the molecular weights and ratios of PEG to use in their compositions, but one of ordinary skill in the art would be aware of the teachings of Szoka, and would be motivated to use these molecular weights and ratios of PEG as a starting point in optimization of the complexes because the compositions of Szoka are very similar in structure and function to those of Yin and Tomalia. For example, the compositions all comprise cationic polyamines with primary amino groups involved in a charge interaction with a nucleic acid and a hydrophilic polymer at the periphery of the polymer, and the intended use of the compositions is the delivery of nucleic acids to cells.

It would have been obvious to one of ordinary skill in the art at the time of the invention to prepare the PEI/DNA/PEG complexes of Yin and Tomalia by first mixing the DNA and PEI, and then adding the PEG. One would have been motivated to take this approach because Szoka teaches that PEG is useful as a masking agent which shields DNA from degradation. As such, it would be obvious to add it to the complex after addition of DNA, thereby maximizing the likelihood that the DNA would be masked. It would have been similarly obvious to use DNA concentrations of about 5-50 or 10-40 μg/ml at a salt concentration below the physiological value in this process because Yin and Tomalia both teach the use of DNA at a concentration of 50 μg/ml in water for the formation of complexes. The use of deionized water is standard operating procedure in molecular biology laboratories, as is well known by one of ordinary skill in the art. Further optimization of the concentration of the complexes for the purpose of transfection is well within the ability of one of ordinary skill in the art, and could reasonably be expected to lead to compositions with the characteristics of claims 63 and 64. The concentration of the complexes can be viewed as a result-effective variable which is routine in the art to optimize.

Thus the invention as a whole was *prima facie* obvious.

Response to Arguments

Applicant's arguments filed 1/17/01 have been fully considered but they are not persuasive.

Applicant's argues that Yin, Tomalia, and Szoka fail to teach normal branched or linear PEI polymers, or " the type of PEI used in the claimed invention". This is irrelevant because the

claims do not recite normal branched or linear PEI polymers, or limit the type of PEI which can be used in the invention..

Applicant argues that there is no motivation to combine Yin and Szoka. Specifically, Applicant argues that the molecular weights and ratios of hydrophilic polymer to primary amine groups disclosed by Szoka would not provide a suitable starting point for the optimization of this ratio in the invention of Yin. This argument is based on the assertion that the polyamidoamine of Szoka, while chemically similar to the PEI of Yin and Tomalia, is likely to have a different protonation state at physiological pH. This assertion is unsupported by evidence, and in any event, Applicant has failed to show that any difference would be significant enough to warrant choosing different ratios than those disclosed by Szoka.

Applicant argues that Yin teaches away from modifying PEI with PEG because Yin suggests modification with PAMAM. This does not constitute teaching away. If Yin stated that modification with PEG led to an inoperable invention, then that would constitute teaching away. Yin does not teach that PEG modification leads to an inoperable invention. Rather, Yin claims a composition of PEI modified with PEG, see claim 12 column 49.

Applicant argues that neither Tomalia nor Yin teach covalent modification of PEI with PEG. These arguments were addressed above. Both these references teach covalent attachment. See Fig.14, step 3 of Yin, and column 17, lines 45-48 of Tomalia.

With respect to claim 64, Applicant argues that it would not have been obvious to concentrate the compositions of Tomalia or Yin to the range of 200ug-1mg/ml because this would

"most likely lead to undesirable aggregation of the complexes". This assertion is unsupported by evidence.

For these reasons the rejections are maintained.

Claim 52 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Yin or Tomalia et al, either one in view of Szoka, as applied to claims 44-51, and 64 above, and further in view of Bogdanov et al (US Patent 5,871,710, effective filing date of 6/17/94) for the reasons of record in Paper No. 6.

The teachings of Szoka and either of Yin or Tomalia can be combined to disclose a complex comprising PEI, DNA, a hydrophilic polymer covalently bound to PEI, and a targeting ligand bound to PEI. These references do not teach a targeting ligand bound to the hydrophilic polymer which is bound to PEI.

Bogdanov teaches a drug delivery composition comprising PEI to which PEG has been covalently attached as a protectant. See column 5, lines 10-16, and 59-60. The composition may also comprise a targeting group bound to either PEI or PEG. See column 6, lines 36-40.

It would have been obvious to one of ordinary skill in the art to attach the targeting ligand of Szoka and either Yin or Tomalia to the hydrophilic polymer rather than to PEI, because Bogdanov suggests doing so. One would have been motivated to do this in order to expose the targeting ligand and to thereby ensure that the targeting ligand is not sterically shielded from the target.

Thus the invention as a whole was *prima facie* obvious.

Response to Arguments

Applicant's arguments filed 1/17/01 have been fully considered but they are not persuasive.

Applicant's arguments regarding Yin, Tomalia, and Szoka are addressed above.

Applicant argues that Bogdanov cannot be properly combined with these references because Bogdanov teaches compositions of different structure and function. In response, the Examiner asserts that Bogdanov teaches the modification of PEG with a targeting ligand, wherein the PEG is covalently bound to PEI. Applicant has provided no evidence that the structure of the complexes of Bogdanov would inhibit one of skill in the art from similarly modifying the PEG of Yin or Tomalia, which is also covalently attached to PEI. For this reason the rejection is maintained.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached on Mondays and Thursdays between the hours of 6:20 AM and 3:50 PM, and on Tuesdays, Wednesdays and Fridays between the hours of 7:00 AM and

4:30 PM (Eastern time). The examiner is off every other Friday, but is usually in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jasemine Chambers, can be reached at 703-308-2035. The FAX phone numbers for art unit 1632 are 703-308-4242 and 703-305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is 703-308-0196.

Scott D. Priebe

Richard Schnizer, Ph. D.

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER